Connecting via Winsock to STN

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LOGINID:SSSPTA1623PAZ

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 21	IPC search and display fields enhanced in CA/CAplus with the IPC reform
NEWS 4	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 5	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 6	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 7	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 8	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 9	JAN 30	Saved answer limit increased
NEWS 10	JAN 31	Monthly current-awareness alert (SDI) frequency added to TULSA
NEWS 11	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 12	FEB 22	Status of current WO (PCT) information on STN
NEWS 13	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 14	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 15	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 16	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 17	FEB 28	TOXCENTER reloaded with enhancements
NEWS 18	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 19	MAR 01	INSPEC reloaded and enhanced
NEWS 20	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 21	MAR 08	X.25 communication option no longer available after June 2006
NEWS 22	MAR 22	EMBASE is now updated on a daily basis

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

NEWS HOURS STN Operating Hours Plus Help Desk Availability
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```
  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 07:13:01 ON 03 APR 2006

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 07:13:21 ON 03 APR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   31 MAR 2006  HIGHEST RN 878899-57-1
DICTIONARY FILE UPDATES:  31 MAR 2006  HIGHEST RN 878899-57-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

*********************************************************************
*                                                                   *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                   *
*********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Documents and Settings\PZucker\My Documents\Examination Auxillary
files\10500101\10500101  clm 2 core.str
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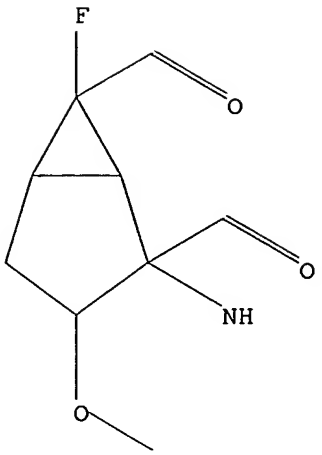
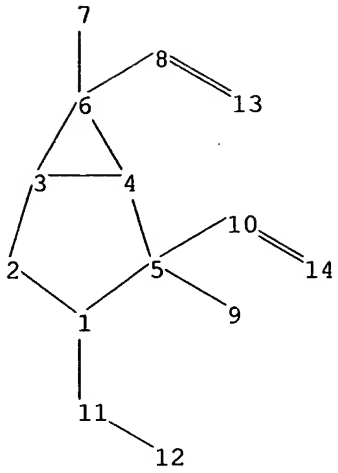


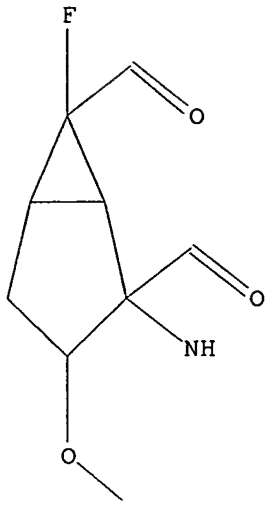


chain nodes :
7 8 9 10 11 12 13 14
ring nodes :
1 2 3 4 5 6
chain bonds :
1-11 5-9 5-10 6-7 6-8 8-13 10-14 11-12
ring bonds :
1-2 1-5 2-3 3-4 3-6 4-5 4-6
exact/norm bonds :
1-2 1-5 1-11 2-3 3-4 3-6 4-5 4-6 5-9 8-13 10-14 11-12
exact bonds :
5-10 6-7 6-8

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

```
=> search l1 sss sam
SAMPLE SEARCH INITIATED 07:13:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       12 TO ITERATE

100.0% PROCESSED       12 ITERATIONS                                  9 ANSWERS
SEARCH TIME: 00.00.01

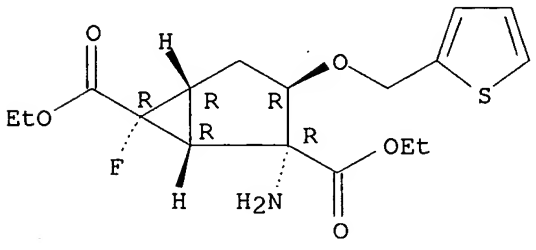
FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           33 TO      447
PROJECTED ANSWERS:               9 TO      360

L2            9 SEA SSS SAM L1

=> d scan

L2   9 ANSWERS   REGISTRY  COPYRIGHT 2006 ACS on STN
IN   Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(2-
     thienylmethoxy)-, diethyl ester, (1R,2R,3R,5R,6R)- (9CI)
MF   C17 H22 F N O5 S
CI   COM

Absolute stereochemistry.  Rotation (+).
```

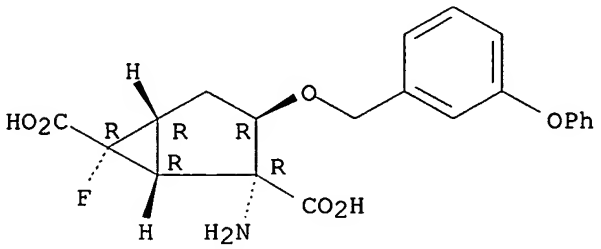


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):9

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-phenoxyphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (9CI)
MF C21 H20 F N O6

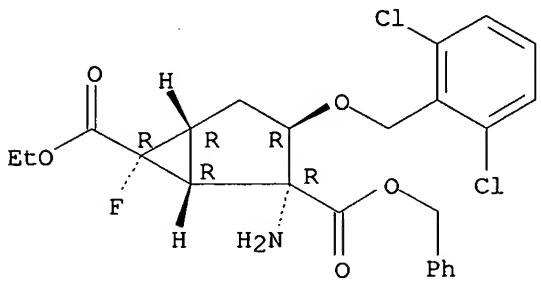
Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,6-dichlorophenyl)methoxy]-6-fluoro-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)- (9CI)
MF C24 H24 Cl2 F N O5

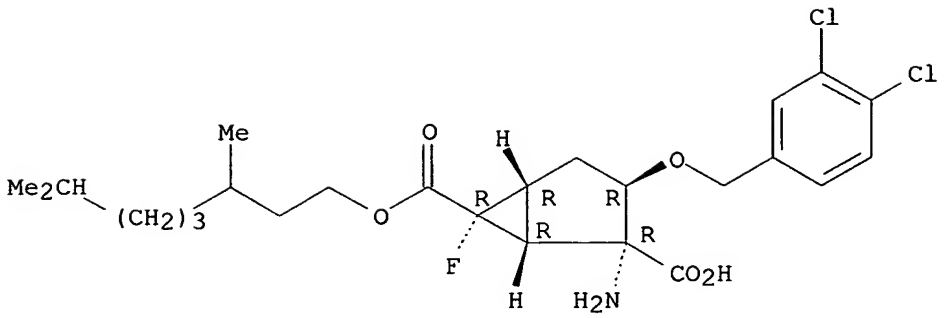
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-(3,7-dimethyloctyl) ester, (1R,2R,3R,5R,6R)- (9CI)
MF C25 H34 Cl2 F N O5

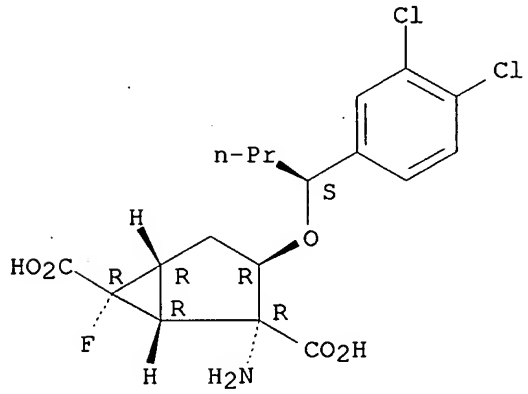
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(1S)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI)
MF C18 H20 Cl2 F N O5

Absolute stereochemistry. Rotation (+).

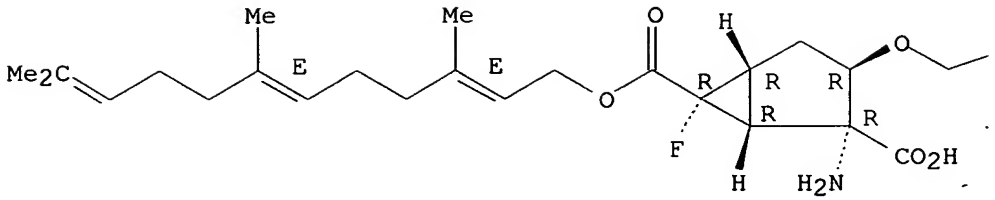


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

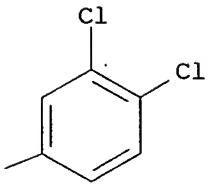
L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl] ester, (1R,2R,3R,5R,6R)- (9CI)
MF C30 H38 Cl2 F N O5

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



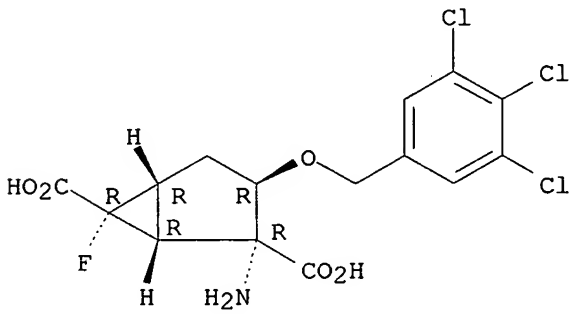
PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3,4,5-trichlorophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (9CI)
MF C15 H13 Cl3 F N O5

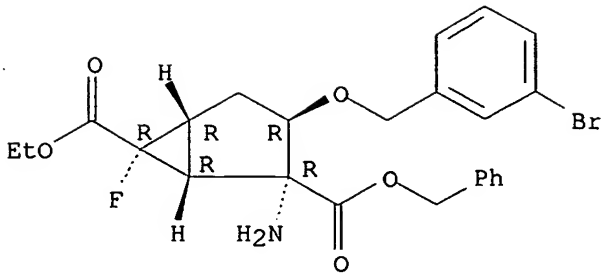
Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-bromophenyl)methoxy]-6-fluoro-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)- (9CI)
MF C24 H25 Br F N O5
CI COM

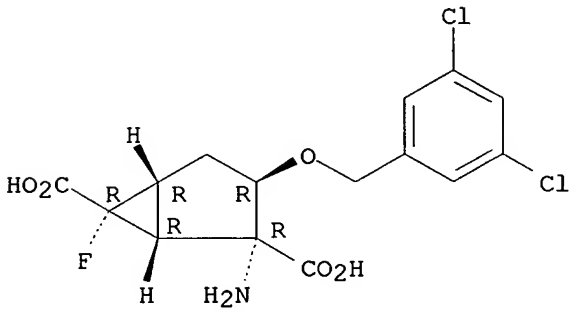
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI)
MF C15 H14 Cl2 F N O5

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.88	1.09

FILE 'CAPLUS' ENTERED AT 07:14:15 ON 03 APR 2006
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FILE COVERS 1907 - 3 Apr 2006 VOL 144 ISS 15
FILE LAST UPDATED: 2 Apr 2006 (20060402/ED)


```
=> l2
L3            4 L2

=> d l3 1-4 ti fbib abs

L3   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esters as
     Group II metabotropic glutamate receptor antagonists
AN   2005:14355  CAPLUS
DN   142:113634
TI   Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esters as
     Group II metabotropic glutamate receptor antagonists
IN   Yasuhara, Akito; Sakagami, Kazunari; Ohta, Hiroshi; Nakazato, Atsuro
PA   Taisho Pharmaceutical Co., Ltd., Japan
SO   PCT Int. Appl., 144 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     ----------          ----   --------    --------------------     --------
PI   WO 2005000791        A1    20050106    WO 2004-JP9398           20040625
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS; JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
                                             JP 2003-181930      A  20030626
                                             JP 2003-373511      A  20031031
                                             JP 2004-128663      A  20040423
     AU 2004252017        A1    20050106    AU 2004-252017         20040625
                                             JP 2003-181930      A  20030626
                                             JP 2003-373511      A  20031031
                                             JP 2004-128663      A  20040423
                                             WO 2004-JP9398      W  20040625
     CA 2530706           AA    20050106    CA 2004-2530706        20040625
                                             JP 2003-181930      A  20030626
                                             JP 2003-373511      A  20031031
                                             JP 2004-128663      A  20040423
                                             WO 2004-JP9398      W  20040625
     EP 1637517           A1    20060322    EP 2004-746867         20040625
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
                                             JP 2003-181930      A  20030626
                                             JP 2003-373511      A  20031031
                                             JP 2004-128663      A  20040423
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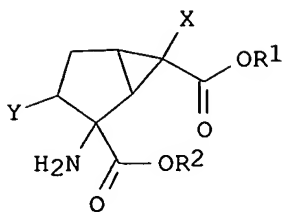
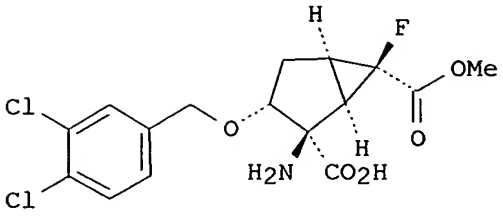
WO 2004-JP9398 W 20040625

OS MARPAT 142:113634
GI



I



II

AB The title compds. I [wherein R1 and R2 = independently alkyl, alkenyl, alkynyl, etc.; X = H or F; Y = (un)substituted alkoxy, SH, amino, etc.] or hydrates or pharmaceutically acceptable salts thereof are prepared as Group II metabotropic glutamate receptor antagonists. For example, the compound II was prepared in a multi-step synthesis. II showed antagonistic effect on Group II metabotropic glutamate receptor in rat. I are useful for the treatment of schizophrenia, anxiety, and diseases related to these, i.e., psychiatrical disorders such as depression, bipolar disorder, and epilepsy (no data).

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
TI mGluR2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivatives for treatment of nervous system diseases
AN 2004:1038326 CAPLUS
DN 142:16843
TI mGluR2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivatives for treatment of nervous system diseases
IN Nakazato, Atsuro; Taki, Shigeyuki; Sakagami, Kazunari; Dean, Reiko; Ota, Hiroyuki; Hirota, Shiho; Yasuhara, Akitaka
PA Taisho Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 70 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
PI	JP 2004339199	A2	20041202	JP 2004-86153		20040324
				JP 2003-117907	A	20030423

OS MARPAT 142:16843
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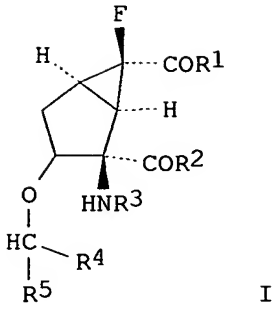
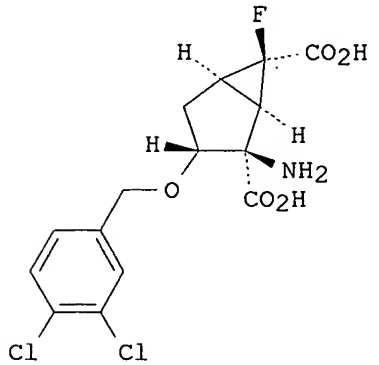


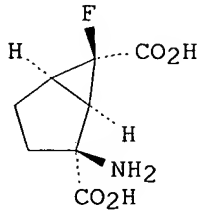
I

AB The antidepressant mGlur2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivs., salts, and hydrates are claimed for treatment of nervous system diseases, including bipolar affective disorder, psychiatry disorder, anxiety, epilepsy, drug dependence, cognition disorder, Alzheimer's disease, Huntington's disease, Parkinson disease, muscle stiffness, brain ischemia, spinal cord injury, head injury, etc.

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
TI Synthesis, in vitro pharmacology, structure-activity relationships, and pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as potent and selective group II metabotropic glutamate receptor antagonists
AN 2004:620394 CAPLUS
DN 141:243074
TI Synthesis, in vitro pharmacology, structure-activity relationships, and pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as potent and selective group II metabotropic glutamate receptor antagonists
AU Nakazato, Atsuro; Sakagami, Kazunari; Yasuhara, Akito; Ohta, Hiroshi; Yoshikawa, Ryoko; Itoh, Manabu; Nakamura, Masato; Chaki, Shigeyuki
CS Medicinal Chemistry Laboratory, Taisho Pharmaceutical Co. Ltd., Kita-ku, Saitama-shi, Saitama, 331-9530, Japan
SO Journal of Medicinal Chemistry (2004), 47(18), 4570-4587
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 141:243074
GI



I



II

AB Group II metabotropic glutamate receptor (mGluR) antagonists,

3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., e.g., I, were discovered by the incorporation of a hydroxy or alkoxyl group onto the C-3 portion of selective and potent group II mGluR agonist II. Among these compds., I (MGS0039) was a highly selective and potent group II mGluR antagonist with the best pharmacokinetic profile. I exhibited high affinities for mGlu 2 (Ki = 2.38 ± 0.40 nM) and mGlu 3 (4.46 ± 0.31 nM) but low affinity for mGluR 7 (Ki = 664 ± 106 nM), and potent antagonist activities for mGlu 2 (IC50 = 20.0 ± 3.67nM) and mGluR 3 (IC50 = 24.0 ± 3.54 nM) but much less potent antagonist activities for mGlu 4 (IC50 = 1740 ± 1080 nM), mGlu 6 (IC50 = 2060 ± 1270 nM), mGlu 1 (IC50 = 93300 ± 14600 nM), and mGluR 5 (IC50 = 117000 ± 38600 nM). No significant agonist activities of I were found for mGluRs 2, 3, 4, 6, 1, and 5 (EC50 > 100000 nM). Furthermore, I exhibited dose-dependent oral absorption (plasma Cmax: 214 ± 56.7, 932 ± 235, and 2960 ± 1150 ng/mL for 3 mg/kg, 10 mg/kg, and 30 mg/kg, po, resp.) and acceptable blood-brain barrier penetration (brain Cmax: 13.2 ng/mL for 10 mg/kg, po 6 h). The synthesis, in vitro pharmacol. profile, and structure-activity relationships of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., and pharmacokinetic profiles of several typical compds, are presented.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
TI 6-Fluorobicyclo[3.1.0]hexane derivatives
AN 2003:591035 CAPLUS
DN 139:143973
TI 6-Fluorobicyclo[3.1.0]hexane derivatives
IN Nakazato, Atsuro; Chaki, Shigeyuki; Sakagami, Kazunari; Dean, Ryoko; Ohta, Hiroshi; Hirota, Shiho; Yasuhara, Akito
PA Taisho Pharmaceutical Co.,ltd., Japan
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
PI	WO 2003061698	A1	20030731	WO 2002-JP13693		20021226
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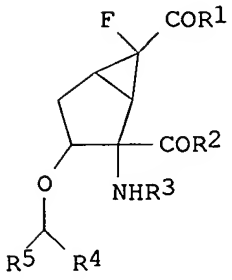

I

AB Antidepressants containing as the active ingredient compds. having group II metabotropic glutamate receptor antagonism; and 2-amino-3-alkoxy-6-fluorobicyclo[3.1.0]- hexane-2,6-dicarboxylic acid derivs. represented by the general formula [I], pharmaceutically acceptable salts thereof, or hydrates of the salts: I wherein R1 and R2 may be the same or different from each other and are each hydroxyl, C1-10 alkoxy, or the like; R3 is C1-10 acyl, C1-6 alkoxy-C1-6 acyl, or the like; and R4 and R5 may be the same or different from each other and are each hydrogen, C1-10 alkyl, or the like.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> search l1 sss samfile reg
REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 07:19:40 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 12 TO ITERATE

100.0% PROCESSED 12 ITERATIONS 9 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:	ONLINE	**COMPLETE**	
	BATCH	**COMPLETE**	
PROJECTED ITERATIONS:		33 TO	447
PROJECTED ANSWERS:		9 TO	360

L4 9 SEA SSS SAM L1

L5 4 L4

MISSING OPERATOR L5 SSS
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.46	17.09

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STRUCTURE FILE UPDATES: 31 MAR 2006 HIGHEST RN 878899-57-1
DICTIONARY FILE UPDATES: 31 MAR 2006 HIGHEST RN 878899-57-1

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when
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*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
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Structure search iteration limits have been increased. See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

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=> search l1 full
ENTER TYPE OF SEARCH (SSS), CSS, FAMILY, OR EXACT:sss
FULL SEARCH INITIATED 07:20:25 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 280 TO ITERATE

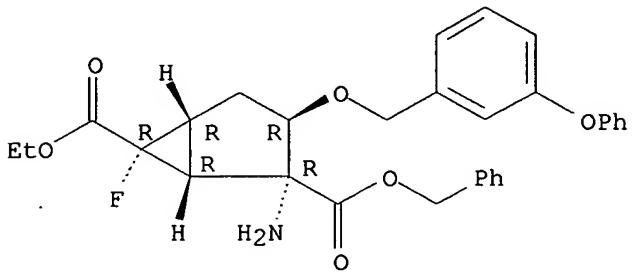
100.0% PROCESSED 280 ITERATIONS 224 ANSWERS
SEARCH TIME: 00.00.01

L6 224 SEA SSS FUL L1

=> d scan

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-phenoxyphenyl)methoxy]-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)-(9CI)
MF C30 H30 F N O6
CI COM

Absolute stereochemistry.

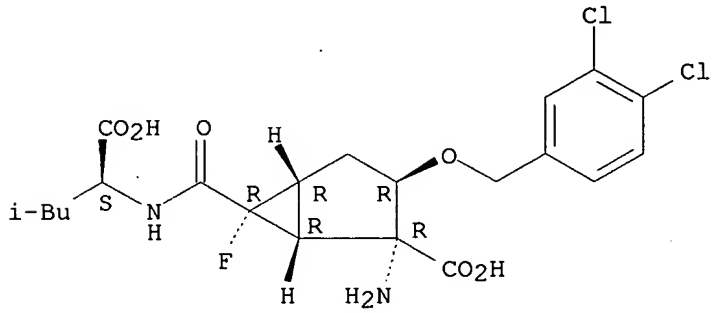


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):20

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2-carboxylic acid, 2-amino-6-[[[(1S)-1-carboxy-3-methylbutyl]amino]carbonyl]-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI)
MF C21 H25 Cl2 F N2 O6

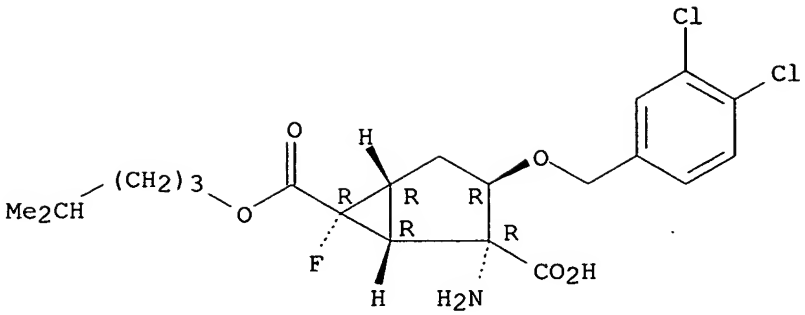
Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-(4-methylpentyl) ester, (1R,2R,3R,5R,6R)- (9CI)
MF C21 H26 Cl2 F N O5

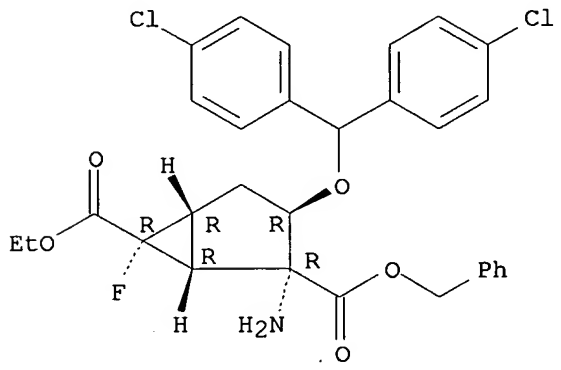
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-chlorophenyl)methoxy]-6-fluoro-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)- (9CI)
MF C30 H28 Cl2 F N O5
CI COM

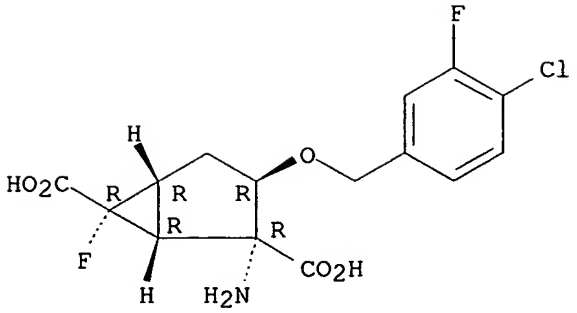
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(4-chloro-3-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI)
MF C15 H14 Cl F2 N O5

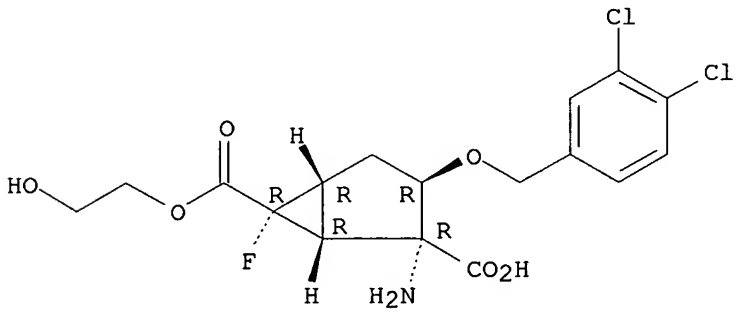
Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-(2-hydroxyethyl) ester, (1R,2R,3R,5R,6R)- (9CI)
MF C17 H18 Cl2 F N O6

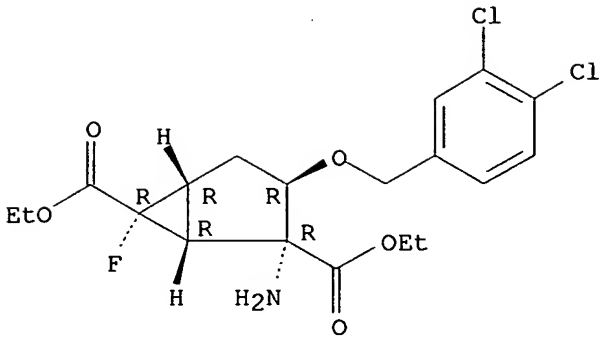
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, diethyl ester, monosodium salt, (1R,2R,3R,5R,6R)- (9CI)
MF C19 H22 Cl2 F N O5 . Na

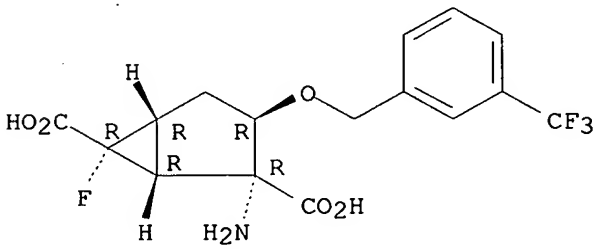
Absolute stereochemistry. Rotation (+).



● Na

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[[3-(trifluoromethyl)phenyl]methoxy]-, (1R,2R,3R,5R,6R)- (9CI)
MF C16 H15 F4 N O5

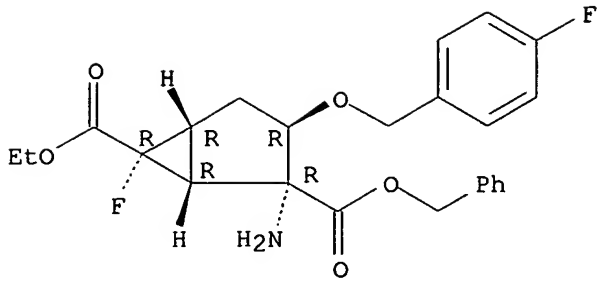
Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(4-fluorophenyl)methoxy]-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)-(9CI)
MF C24 H25 F2 N O5
CI COM

Absolute stereochemistry.



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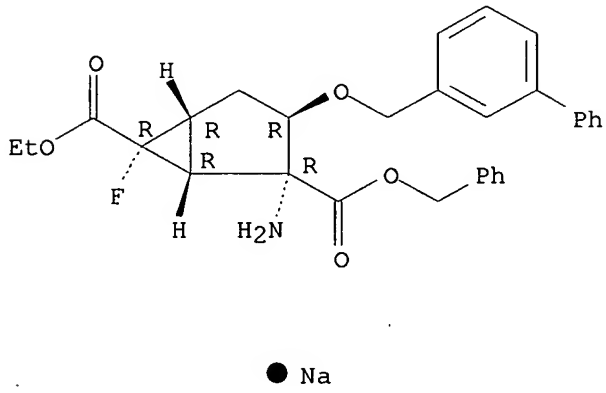
L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-([1,1'-biphenyl]-3-ylmethoxy)-6-fluoro-, 6-ethyl 2-(phenylmethyl) ester, monosodium salt, (1R,2R,3R,5R,6R)- (9CI)
MF C30 H30 F N O5 . Na

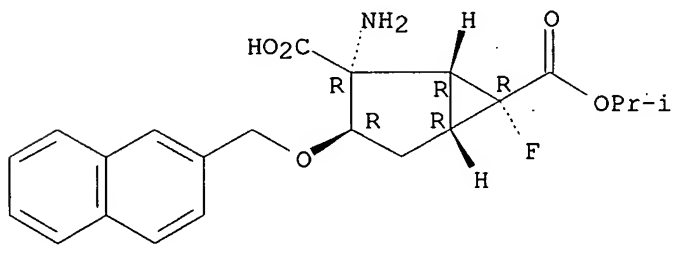
Absolute stereochemistry.



● Na

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(2-naphthalenylmethoxy)-, 6-(1-methylethyl) ester, (1R,2R,3R,5R,6R)- (9CI)
MF C22 H24 F N O5

Absolute stereochemistry.



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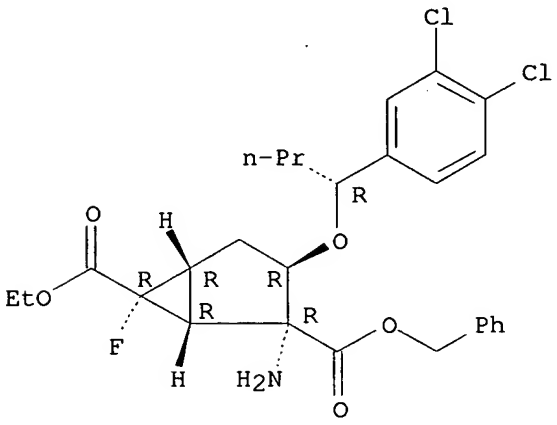
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(1R)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)- (9CI)
MF C27 H30 Cl2 F N O5
CI COM

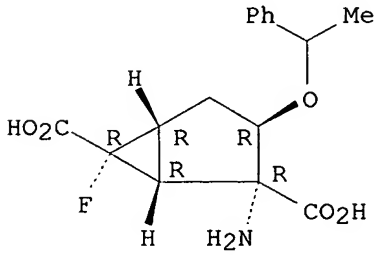
Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(1-phenylethoxy)-, (1R,2R,3R,5R,6R)- (9CI)
MF C16 H18 F N O5

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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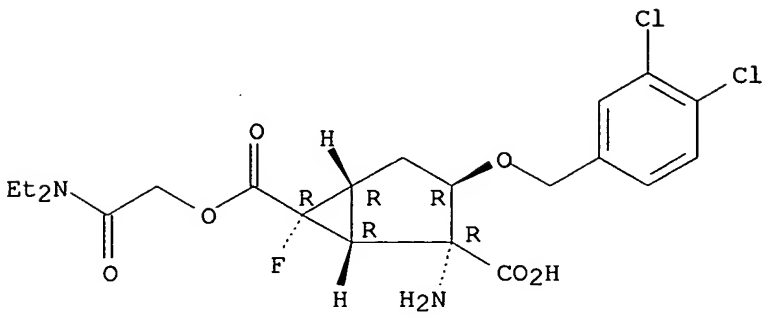
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-

dichlorophenyl)methoxy]-6-fluoro-, 6-[2-(diethylamino)-2-oxoethyl] ester, (1R,2R,3R,5R,6R)- (9CI)
MF C21 H25 Cl2 F N2 O6

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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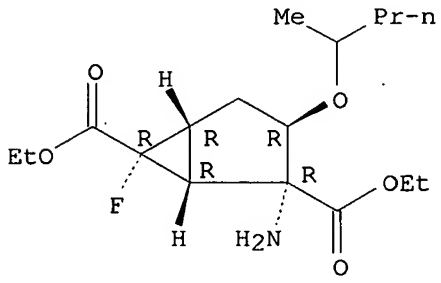
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(1-methylbutoxy)-, diethyl ester, monosodium salt, (1R,2R,3R,5R,6R)- (9CI)
MF C17 H28 F N O5 . Na

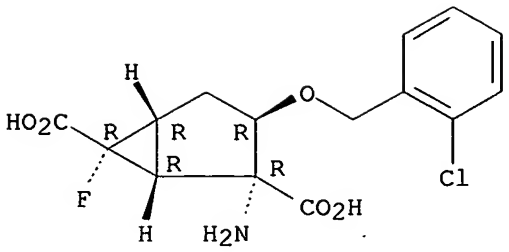
Absolute stereochemistry.



● Na

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI)
MF C15 H15 Cl F N O5

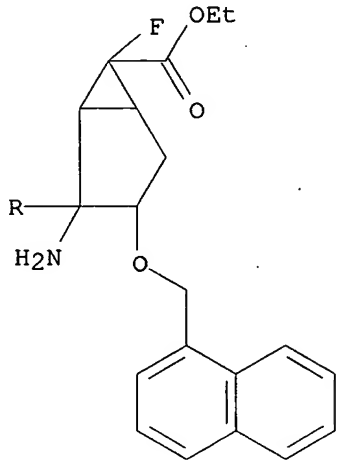
Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(1-naphthalenylmethoxy)-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)-(9CI)
MF C28 H28 F N O5
CI COM

PAGE 1-A



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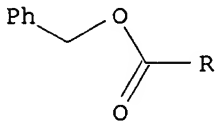
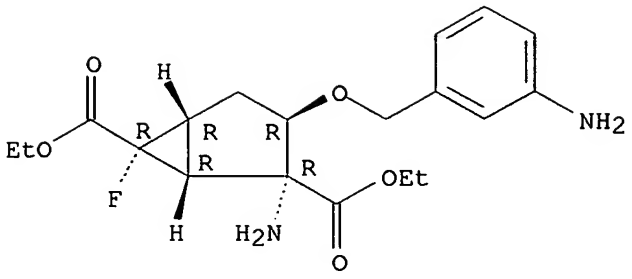


L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-aminophenyl)methoxy]-6-fluoro-, diethyl ester, monosodium salt, (1R,2R,3R,5R,6R)- (9CI)
MF C19 H25 F N2 O5 . Na

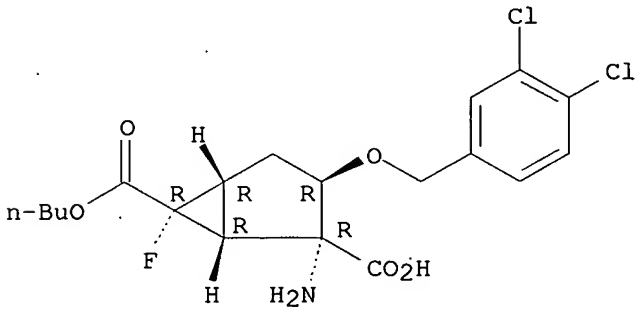
Absolute stereochemistry. Rotation (-).



● Na

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-butyl ester, (1R,2R,3R,5R,6R)- (9CI)
MF C19 H22 Cl2 F N O5
CI COM

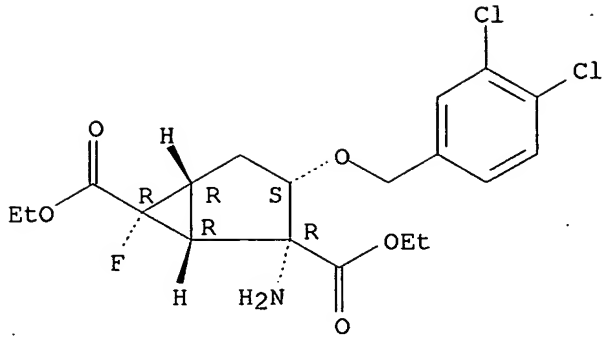
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, diethyl ester, (1R,2R,3S,5R,6R)- (9CI)
MF C19 H22 Cl2 F N O5

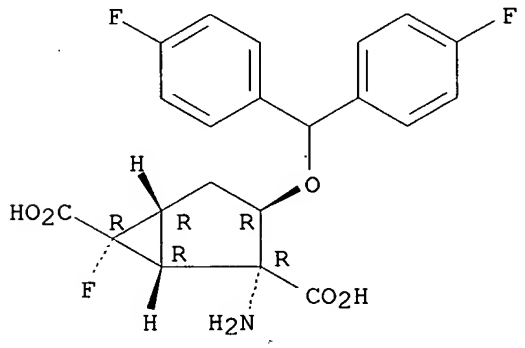
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI)
MF C21 H18 F3 N O5

Absolute stereochemistry. Rotation (-).



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FULL ESTIMATED COST	167.38	184.47

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-3.00

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L7          11 L6

=> d his

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L3            4 L2
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     FILE 'REGISTRY' ENTERED AT 07:19:40 ON 03 APR 2006
L4            9 S L1

     FILE 'CAPLUS' ENTERED AT 07:19:40 ON 03 APR 2006
L5            4 S L4

     FILE 'REGISTRY' ENTERED AT 07:19:51 ON 03 APR 2006
L6          224 SEARCH L1 FULL SSS

     FILE 'CAPLUS' ENTERED AT 07:21:12 ON 03 APR 2006
L7           11 L6

=> l7 not l5
L8            7 L7 NOT L5

=> d l8 1-7 ti fbib abs

L8   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   A metabotropic glutamate 2/3 receptor antagonist, MGS0039, increases
     extracellular dopamine levels in the nucleus accumbens shell
AN   2005:1351480  CAPLUS
DN   144:81056
TI   A metabotropic glutamate 2/3 receptor antagonist, MGS0039, increases
     extracellular dopamine levels in the nucleus accumbens shell
AU   Karasawa, Jun-ichi; Yoshimizu, Takao; Chaki, Shigeyuki
CS   Medicinal Pharmacology Laboratory, Medicinal Research Laboratories, Taisho
     Pharmaceutical Co., Ltd., Kita-ku, Saitama, 331-9530, Japan
SO   Neuroscience Letters (2006), 393(2-3), 127-130
     CODEN: NELED5; ISSN: 0304-3940
PB   Elsevier Ltd.
```

DT Journal
LA English
AB MGS0039, a potent and selective metabotropic glutamate 2/3 (mGlu 2/3) receptor antagonist, exhibits antidepressant-like activities in some animal models. In the present study, the authors examined the effect of MGS0039 on extracellular dopamine levels in the rat nucleus accumbens (NAc) shell using in vivo microdialysis evaluation because accumbal dopamine has been implicated in depression. Local application of MGS0039 into the NAc shell at 10 μM significantly increased extracellular dopamine levels in the NAc shell in freely moving rats. In contrast, local application of 10 μM of LY354740, an mGlu 2/3 receptor agonist, significantly decreased extracellular dopamine levels in the same brain region. These findings suggest that dopamine release in the NAc shell is regulated by mGlu 2/3 receptors, and that the effect on dopamine levels in the NAc shell may partially explain the antidepressant-like properties of mGlu 2/3 receptor antagonists.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
TI AMPA receptor stimulation mediates the antidepressant-like effect of a group II metabotropic glutamate receptor antagonist
AN 2005:298938 CAPLUS
DN 142:423678
TI AMPA receptor stimulation mediates the antidepressant-like effect of a group II metabotropic glutamate receptor antagonist
AU Karasawa, Jun-Ichi; Shimazaki, Toshiharu; Kawashima, Naoya; Chaki, Shigeyuki
CS Medicinal Pharmacology Laboratory, Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Saitama, 331-9530, Japan
SO Brain Research (2005), 1042(1), 92-98
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier B.V.
DT Journal
LA English
AB (1R,2R,3R,5R,6R)-2-Amino-3-(3,4-dichlorobenzyloxy)-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid (MGS0039), a selective group II metabotropic glutamate receptor (mGluR) antagonist, exhibits antidepressant-like activities in rodent models. In the present studies, to clarify the involvement of α-amino-3-hydroxy-5-methylisoxazole-4-propionate (AMPA) receptor activation in exhibition of the antidepressant-like properties of MGS0039, the authors examined the effect of an AMPA receptor antagonist, 2,3-dihydroxy-6-nitro-7-sulfamoylbenzo(f)quinoxaline (NBQX), on the antidepressant-like effect of MGS0039 in the mouse tail suspension test. The authors also examined the effects of NBQX on increased serotonin release after treatment with MGS0039 in the rat medial prefrontal cortex (mPFC) using in vivo microdialysis evaluation. In the tail suspension test, MGS0039 (0.3-3 mg/kg, i.p.) treatment dose-dependently and significantly reduced immobility time. Pretreatment with NBQX (10 mg/kg, s.c.) significantly prevented the antidepressant-like effect of MGS0039 in the tail suspension test, while NBQX itself had no effect on immobility time. In the microdialysis evaluation, administration of MGS0039 (10 mg/kg, i.p.) significantly increased serotonin levels in mPFC in freely moving rats, while NBQX (1 mg/kg, i.p.) itself had no effect on serotonin release in this region. Pretreatment with NBQX significantly attenuated the increase in serotonin release by MGS0039. These findings suggest that stimulation of postsynaptic AMPA receptors plays a role in mediating the pharmacol. effects of MGS0039.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

TI Neuropharmacological profiles of antagonists of group II metabotropic glutamate receptors
AN 2005:234178 CAPLUS
DN 142:367493
TI Neuropharmacological profiles of antagonists of group II metabotropic glutamate receptors
AU Kawashima, Naoya; Karasawa, Jun-ichi; Shimazaki, Toshiharu; Chaki, Shigeyuki; Okuyama, Shigeru; Yasuhara, Akito; Nakazato, Atsuro
CS Research Strategy Group, Pharmaceutical Business Division, Taisho Pharmaceutical Co., Ltd., Saitama, Saitama, 331-9530, Japan
SO Neuroscience Letters (2005), 378(3), 131-134
CODEN: NELED5; ISSN: 0304-3940
PB Elsevier Ltd.
DT Journal
LA English
AB Glutamatergic abnormalities play roles in several psychiatric disorders. Glutamate acts at two classes of receptors, ionotropic and metabotropic glutamate receptors (mGluR), the latter is classified into three group, based on receptor homol. and signaling mechanisms. Among them, recent pharmacol. and histochem. studies suggest that the group II mGluR (mGluR2 and mGluR3) plays crucial roles in the control of emotional states. We previously reported that MGS0039, a selective group II mGluR antagonist, exhibited dose-dependent antidepressant-like effects in some animal models. However, the mechanism by which group II mGluR antagonists exhibit such effects is still unclear. In the present two studies, we examined neuropharmacol. effects of group II mGluR antagonists on monoaminergic neurons. In an electrophysiol. study, MGS0039 dose-dependently and significantly increased the firing rate of dorsal raphe nucleus (DRN) serotonergic neurons. LY341495, another group II mGluR antagonist, also increased DRN serotonergic neural activity significantly. Consistent with the findings of this electrophysiol. study, MGS0039 significantly increased extracellular level of serotonin in rat medial prefrontal cortex in a microdialysis study. In contrast, MGS0039 had no effect on the activity of locus coeruleus noradrenergic neurons. These findings suggest that modulation of serotonergic neuron might be, at least in part, responsible for the antidepressant-like effects of group II mGluR antagonists.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
TI Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as antagonists of group II metabotropic glutamate receptor
AN 2005:14354 CAPLUS
DN 142:113754
TI Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as antagonists of group II metabotropic glutamate receptor
IN Yasuhara, Akito; Sakagami, Kazunari; Ohta, Hiroshi; Nakazato, Atsuro
PA Taisho Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005000790	A1	20050106	WO 2004-JP9384	20040625

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2003-181931 A 20030626

OS MARPAT 142:113754

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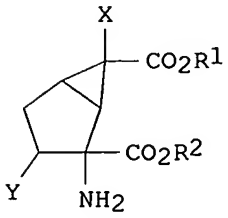
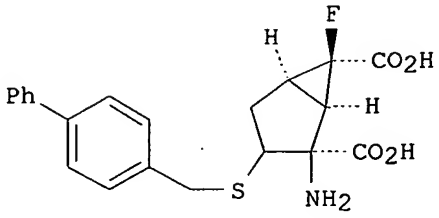


I



II

AB The title compds. [I; R1, R2 = H, C1-10 alkyl, Ph, naphthyl, mono- or diphenyl-C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, hydroxy-C2-10 alkyl, C1-10 alkoxycarbonyl-C1-10 alkyl, amino-C2-10 alkyl, C1-10 alkoxy-C1-10 alkyl; X = H, F; Y = NH2, SR3, S(O)nR7, SCHR3R4, S(O)nCHR3R4, NHCHR3R4, N(CHR3R4)(CHR5R6), NHCOR3, O2CR7; wherein R3-R6 = H, C1-10 alkyl, (un)substituted Ph, naphthyl, 1-7 halogen(s)-substituted naphthyl, heteroaryl; R7 = C1-10 alkyl, (un)substituted Ph, naphthyl, 1-7 halogen(s)-substituted naphthyl, heteroaryl; n = 1,2], pharmaceutically acceptable salts thereof, or hydrates of either are prepared These compds., e.g. (II), had an antagonistic effect on a Group II metabotropic glutamate receptor with IC50 of ≤200 nM, and are effective in treatments for and prevention of psychiatric disorders and neurol. diseases.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

TI Anxiolytic-like activity of MGS0039, a potent group II metabotropic glutamate receptor antagonist, in a marble-burying behavior test

AN 2004:814656 CAPLUS

DN 141:325597

TI Anxiolytic-like activity of MGS0039, a potent group II metabotropic glutamate receptor antagonist, in a marble-burying behavior test

AU Shimazaki, Toshiharu; Iijima, Michihiko; Chaki, Shigeyuki

CS Psychiatric Diseases and Pain Research, Medicinal Pharmacology Laboratory, Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Saitama, Saitama, 331-9530, Japan

SO European Journal of Pharmacology (2004), 501(1-3), 121-125
CODEN: EJPHAZ; ISSN: 0014-2999

PB Elsevier B.V.

DT Journal

LA English

AB Glutamatergic abnormalities are involved in several psychiatric disorders. Clin. evidence demonstrates altered glutamatergic neurotransmission in patients suffering from obsessive-compulsive disorder. MGS0039, (1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzyloxy)-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid, is a novel group II metabotropic glutamate (mGlu) receptor antagonist. We examined MGS0039's potential anti-obsessive-compulsive disorder activity, using the marble-burying behavior test as a model of obsessive-compulsive disorder. MGS0039 as well as LY341495 ((2S,1'S,2'S)-2-(9-xanthylmethyl)-2-(2'-carboxycycloprolyl)glycine), another group II mGlu receptor antagonist, inhibited marble-burying behavior. We also demonstrated that this effect

was significantly attenuated by a group II mGlu receptor agonist. This data indicates that group II mGlu receptor antagonists may exert anti-obsessive-compulsive disorder effects in clin. use.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
TI MGS0039: a potent and selective group II metabotropic glutamate receptor antagonist with antidepressant-like activity
AN 2004:126085 CAPLUS
DN 141:82129
TI MGS0039: a potent and selective group II metabotropic glutamate receptor antagonist with antidepressant-like activity
AU Chaki, Shigeyuki; Yoshikawa, Ryoko; Hirota, Shiho; Shimazaki, Toshiharu; Maeda, Maoko; Kawashima, Naoya; Yoshimizu, Takao; Yasuhara, Akito; Sakagami, Kazunari; Okuyama, Shigeru; Nakanishi, Shigetada; Nakazato, Atsuro
CS Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Saitama, 331-9530, Japan
SO Neuropharmacology (2004), 46(4), 457-467
CODEN: NEPHBW; ISSN: 0028-3908
PB Elsevier Science B.V.
DT Journal
LA English
AB The present study describes the pharmacol. profile of (1R,2R,3R,5R,6R)-2-Amino-3-(3,4-dichlorobenzyloxy)-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid (MGS0039), a novel group II mGluR antagonist. MGS0039 showed high affinity for both mGluR2 (Ki = 2.2 nM) and mGluR3 (Ki = 4.5 nM), which are comparable to LY341495, another group II mGluR antagonist. MGS0039 attenuated both glutamate-induced inhibition of forskolin-evoked cAMP formation in CHO cells expressing mGluR2 (IC50 = 20 nM) or mGluR3 (IC50=24 nM) and glutamate-increased [35S]GTPγS binding to mGluR2 (pA2=8.2), which means that MGS0039 acts as an antagonist. MGS0039 shifted the dose-response curve of glutamate-increased [35S]GTPγS binding rightward without altering the maximal response, and thereby indicating competitive antagonism. MGS0039 showed no significant effects on other mGluRs as well as the other receptors and transporters we studied. MGS0039 (0.3-3 mg/kg, i.p.) as well as LY341495 (0.1-3 mg/kg, i.p.) had dose-dependent antidepressant-like effects in the rat forced swim test and in the mouse tail suspension test. In contrast, MGS0039 (0.3-3 mg/kg, i.p.) had no apparent effect in the rat social interaction test and in the rat elevated plus-maze. These results indicate that MGS0039 is a potent and selective antagonist of group II mGluR, and that group II mGluR antagonists, like MGS0039, have an antidepressant-like potential in exptl. animal models.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
TI Increased cell proliferation in the adult mouse hippocampus following chronic administration of group II metabotropic glutamate receptor antagonist, MGS0039
AN 2004:96754 CAPLUS
DN 140:368470
TI Increased cell proliferation in the adult mouse hippocampus following chronic administration of group II metabotropic glutamate receptor antagonist, MGS0039
AU Yoshimizu, Takao; Chaki, Shigeyuki
CS Medicinal Research Laboratories, Medicinal Pharmacology Laboratory, Psychiatric Diseases and Pain Research, Taisho Pharmaceutical Co., Ltd., Kita-ku, Saitama, 331-9530, Japan
SO Biochemical and Biophysical Research Communications (2004), 315(2), 493-496

CODEN: BBRCA9; ISSN: 0006-291X
PB Elsevier Science
DT Journal
LA English
AB We have previously reported that MGS0039, a novel antagonist of group II metabotropic glutamate receptors (mGluRs), exerts antidepressant-like effects in exptl. animal models. Recent studies suggest that the behavioral effects of chronic antidepressant treatment are mediated by the stimulation of neurogenesis in the hippocampus. In the present study, we examined the effects of MGS0039 on cell proliferation in the adult mouse hippocampus. MGS0039 (5 or 10 mg/kg) or fluvoxamine was administered chronically to male ICR mice over a period of 14 days. Multiple bromodeoxyuridine (BrdU) administrations were performed after the last drug injection to label dividing cells. Immunohistochem. analyses after BrdU injections revealed that chronic MGS0039 treatment enhanced BrdU-pos. cells in the dentate gyrus (.apprx.62% increase) in the same manner as chronic fluvoxamine treatment. This is the first in vivo study to demonstrate an increase in cell proliferation following a blockade of group II mGluRs. These findings raise the possibility that MGS0039 may exert antidepressant-like effects by modulating cell proliferation in the hippocampus.
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
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NEWS	4	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS	5	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	6	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	7	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	8	JAN 17	IPC 8 in the WPI family of databases including WPIFV

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NEWS 10   JAN 31  Monthly current-awareness alert (SDI) frequency
                  added to TULSA
NEWS 11   FEB 21  STN AnaVist, Version 1.1, lets you share your STN AnaVist
                  visualization results
NEWS 12   FEB 22  Status of current WO (PCT) information on STN
NEWS 13   FEB 22  The IPC thesaurus added to additional patent databases on STN
NEWS 14   FEB 22  Updates in EPFULL; IPC 8 enhancements added
NEWS 15   FEB 27  New STN AnaVist pricing effective March 1, 2006
NEWS 16   FEB 28  MEDLINE/LMEDLINE reload improves functionality
NEWS 17   FEB 28  TOXCENTER reloaded with enhancements
NEWS 18   FEB 28  REGISTRY/ZREGISTRY enhanced with more experimental spectral
                  property data
NEWS 19   MAR 01  INSPEC reloaded and enhanced
NEWS 20   MAR 03  Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 21   MAR 08  X.25 communication option no longer available after June 2006
NEWS 22   MAR 22  EMBASE is now updated on a daily basis

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              CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
              V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
              http://download.cas.org/express/v8.0-Discover/

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=> metabotropic glutamate
          5879 METABOTROPIC
        100447 GLUTAMATE
          1102 GLUTAMATES
        100846 GLUTAMATE
                 (GLUTAMATE OR GLUTAMATES)
L1        4363 METABOTROPIC GLUTAMATE
                 (METABOTROPIC(W)GLUTAMATE)

=> ?depress?
L2      196569 ?DEPRESS?

=> l1(l)l2
L3         543 L1(L)L2

=> metabotropic glutamate receptor
          5879 METABOTROPIC
        100447 GLUTAMATE
          1102 GLUTAMATES
        100846 GLUTAMATE
                 (GLUTAMATE OR GLUTAMATES)
        643933 RECEPTOR
        590549 RECEPTORS
        766401 RECEPTOR
                 (RECEPTOR OR RECEPTORS)
L4        4123 METABOTROPIC GLUTAMATE RECEPTOR
                 (METABOTROPIC(W)GLUTAMATE(W)RECEPTOR)

=> l2(l)l4
L5         494 L2(L)L4

=> antidepressant
         19799 ANTIDEPRESSANT
         22981 ANTIDEPRESSANTS
L6       27225 ANTIDEPRESSANT
                 (ANTIDEPRESSANT OR ANTIDEPRESSANTS)

=> l3(l)l6
L7          73 L3(L)L6

=> d l7 63-73 ti

L7   ANSWER 63 OF 73  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Physiological antagonism between 5-hydroxytryptamine2a and group II
     metabotropic glutamate receptors in prefrontal cortex

L7   ANSWER 64 OF 73  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   An antidepressant-induced decrease in the responsiveness of
     hippocampal neurons to group I metabotropic glutamate
     receptor activation

L7   ANSWER 65 OF 73  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Potential anti-anxiety, anti-addictive effects of LY 354740, a selective
     group II glutamate metabotropic receptors agonist in animal models

L7   ANSWER 66 OF 73  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Preparation of fluorine-containing amino acid derivatives as group-2
```

metabotropic glutamate receptor agonists

L7 ANSWER 67 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN
TI Extracts and constituents of Hypericum perforatum inhibit the binding of various ligands to recombinant receptors expressed with the Semliki Forest virus system

L7 ANSWER 68 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN
TI Preparation of 5H-thiazolo[3,2-a]pyrimidines as metabotropic glutamate receptor antagonists and/or agonists.

L7 ANSWER 69 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN
TI The electrophysiology of prefrontal serotonin systems: therapeutic implications for mood and psychosis

L7 ANSWER 70 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN
TI Differential effects of electroconvulsive shock on the glutamate receptor mRNAs for NR2A, NR2B and mGluR5b

L7 ANSWER 71 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN
TI Antidepressant treatment influences group I of glutamate metabotropic receptors in slices from hippocampal CA1 region

L7 ANSWER 72 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN
TI Influence of imipramine treatment on the group I of metabotropic glutamate receptors in CA1 region of hippocampus

L7 ANSWER 73 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN
TI Antidepressant treatment influences cyclic AMP accumulation induced by excitatory amino acids in rat brain

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